

Safety and Efficacy of SLT vs ALT - Short and Longer Term Perspectives



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Introduction

Laser treatment of the anterior chamber angle seems to have been first described in 1961 by Zweng and Flocks using a xenon-arc light source in cats, dogs, and monkeys [1]. Laser treatment of the human trabecular mesh work by puncturing Schlemm's canal was performed initially by Krasnov [2], but the lower intraocular pressure (IOP) he described was short-lived [2]. Argon laser trabeculotomy in humans and monkeys was reported by Worthen & Wickham [3]. Subsequently, Ticho & Zuberger noted that Argon laser treatment of the angle was successful in lowering IOP despite lack of permanent trabecular openings [4].

Contemporary use of Argon laser trabeculoplasty (ALT) is based on a report demonstrating safety and efficacy in a group of open-angle glaucoma patients in 1979 by Wise & Witter [5]. In 1998, Latina and colleagues utilized a frequency-doubled neodymium:yttrium - aluminum - garnet (Nd:YAG) non-thermal laser to lower IOP successfully in patients with open-angle glaucoma [6]. This laser works by utilizing selective photothermolysis, selectively targeting melanin and melanin laden cells with minimal collateral damage to adjacent structures, and hence is referred to as selective laser trabeculoplasty (SLT) [7,8].

Although other lasers have been utilized for laser trabeculoplasty, ALT and SLT appear to be the most common methods employed. Very few publications have compared these

two laser modalities, and this review examines evidence for short and longer term efficacy and safety based on these studies [9-20]. One of these studies was pivotal in obtaining FDA approval for the SLT in the USA [21].

Methods

A search for studies comparing SLT to ALT in open angle glaucoma were conducted using PubMed and Google. Key search terms were selective laser trabeculoplasty and argon laser trabeculoplasty and the search was performed on February 14, 2017.

Efficacy

12 studies were found, and of these 2 involved a retrospective comparison, and 10 prospective. 3 of the studies were prospective randomized in design. Other aspects of study characteristics including results are summarized in Table 1. Nearly all treatments involved applying laser to 180 degrees of the meshwork in eyes that had received previous medical therapy. The vast majority of studies had a preponderance of primary open angle glaucoma (POAG) patients compared to other subtypes of glaucoma. All studies conclude that there were no significant differences in IOP lowering between SLT and ALT groups i.e. SLT is equivalent to ALT in short and longer term efficacy.

Table 1: Efficacy of SLT vs ALT: summary of study design, findings, and limitations.

Study	Design/ Glaucoma type	Sample size (eyes)	Duration (longest)	Findings	Limitations
Liu et al. [9]	Prospective randomized control trial; mostly POAG	42 (20 SLT and 22 ALT)	2 years	Significant IOP decrease of 11.1% after ALT (P=0.01) and 7.7% after SLT (P=0.01) with no statistical difference between the lasers (P>0.05)	Small sample size, both eyes treated although only first analyzed. Low mean baseline IOP for both groups prior to laser
Si et al. [10]	Prospective randomized. Only exfoliation patients enrolled.	76 (45 SLT, 31 ALT)	1 year	-6.2 mmHg and -8.6mmHg decrease with SLT and ALT, respectively. No significant difference.	Pretreatment IOP higher for ALT vs SLT (25.2 vs. 23.1 mmHg; p=0.03). 36% loss to follow-up at 1 year.

Bovell et al. [11]	Prospective randomized control trial; mostly POAG with some XFG and PG	176 (89 SLT and 87 ALT)	5 years	Baseline similar in both groups. IOP lowering at 5yrs SLT -7.4 ± 7.3 mmHg vs ALT -6.7 ± 6.6 mmHg; $p=0.298$. Large but similar number of interventions in both groups over study period	Trial not designed for 5 year follow-up. Moderate loss to follow-up (64 SLT eyes remaining and 56 ALT at 5yrs).
Almeida et al. [12]	Prospective, non-randomized interventional case series; mostly POAG	45 (25 SLT and 20 ALT)	6 months	IOP reduction with SLT 5.1 ± 2.5 mmHg and ALT 4.4 ± 2.8 mmHg; $p=0.38$.	Small sample size, non-randomized, short follow-up
Russo et al. [13]	Prospective randomized control trial; mostly POAG	120 (61 SLT, 59 ALT)	12 months	IOP lowering with SLT 6.01 mmHg and ALT 6.12 mmHg $p=0.794$. No significant difference	Small sample size
Best et al. [14]	Prospective non-randomized	165 (124 SLT and 41 ALT)	12 months	Mean pressure reductions 1.8 mmHg (8.5 %) after SLT, and 2.1 mmHg (9.4 %) after ALT. No significant difference	
Damji et al. [15]	Prospective randomized control trial	176 (89 SLT and 87 ALT)	1 year	Decrease in IOP at 1 year for SLT 5.86 mmHg and ALT 6.04 mmHg; $p=0.846$	IOP taken by one individual not masked to treatment. Some treated patients had prior ALT.
Van de veire S et al. [16]	Retrospective interventional case series; mostly POAG	56 (38 SLT and 18 ALT)	3-5 weeks	IOP-reduction was 22.4% after ALT and 15.5% after SLT; $p=0.141$	Small sample size, retrospective design with selection bias as patients preferentially received ALT or SLT depending on TM pigmentation. 4 eyes were excluded from analysis because of post treatment IOP rise.
Juzych et al. [17]	Retrospective chart review; only POAG patients enrolled	195 (41 SLT and 154 ALT)	Mean follow-up 37.4 ± 14.7 months (SLT) and 33.6 ± 17.0 months (ALT)	No statistically significant difference in IOP reduction between two groups using two different success criteria	Retrospective design with selection bias as patients underwent SLT or ALT based on availability
Martinez de la casa et al. [18]	Prospective non-randomized study; only POAG patients enrolled	40 (20 SLT and 20 ALT)	6 months	Reduction in IOP for SLT 22.2% (range 0–36.3%) and ALT 19.5% (range 0–30.2%). $P=0.741$	Small sample size, unclear methodology of how patients assigned to SLT or ALT group
Popiela et al. [19]	Prospective randomized; mostly POAG	27 patients with one eye receiving SLT and the other ALT	3 months	Mean IOP drop -2.85 ± 4.62 mm Hg after SLT and -2.63 ± 3.60 mm Hg after ALT; $p=0.84$. No significant difference in IOP reduction between two groups	Pretreatment IOP higher in ALT eyes vs. SLT (21.3 vs 20.3; $p=0.04$). No control for crossover effect.
Holló [20]	Prospective non-randomized study; mostly POAG	14 patients with one eye receiving SLT and the other ALT	1-18 months	IOP lowering varied between 0-3mm Hg in each eye. No significant difference in IOP lowering between eyes detected.	Small sample size

XFG: Exfoliation Glaucoma; XFS: Exfoliation Syndrome; PG: Pigmentary Glaucoma; POAG Primary Open Angle Glaucoma

Notes: For ALT all studies utilized a 50micron spot size and 0.1msec duration. For SLT all studies utilized a 3nsec pulse and 400 micron spot.

It is worth noting that the effect of SLT and ALT diminishes with time at about the same rate. This is illustrated in the study by Bovell et al. [11] which indicates that time to 50% failure in each group was approximately 2 years [11] (Figure 1). The definition of success employed in this study was 20% IOP lowering with no additional medical, laser, or surgical interventions. The survival rate of persons after having received SLT was 44% at 3 years; at 4 years it was 38%; and at 5 years it was 25%. For patients

who received ALT, survival at 3 years was 37%; at 4 years, 30%; and at 5 years, 27%. It is worth noting that patients enrolled in the study were on maximal tolerated medical therapy, and required a large number of subsequent interventions (laser trabeculoplasty, incisional surgery, and cyclophoto coagulation) in both groups, over the 5-year follow-up period (49/89 SLT and 33/87 ALT eyes).

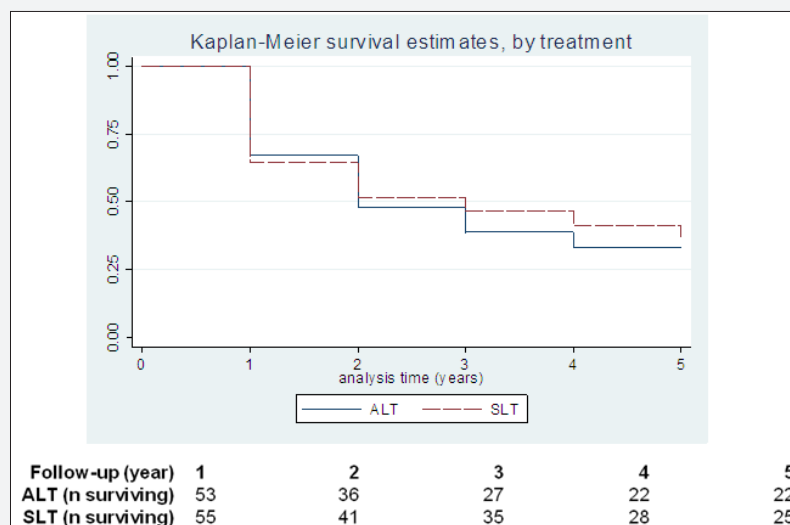


Figure 1: Survival analysis of all patients in the study by Bovell et al. [11]. Success is defined as at least 20% lowering of intraocular pressure with no additional medical, laser, or surgical interventions (reproduced with permission from Elsevier).

Safety

The most common complication reported in clinical studies of laser trabeculoplasty is an increase in IOP with highest spikes occurring within the first hour - although they may be delayed [22]. In a prospective randomized control trial, the reported incidence of increase in IOP greater than 6 mmHg from baseline 1 hour after SLT and ALT in patients who were prophylactically treated for a pressure spike with an alpha adrenergic agonist was 3.4% in ALT-treated eyes and 4.5% in SLT-treated eyes [15]. These spikes typically resolve quickly with the addition of IOP lowering therapy [23]. If no prophylactic agent was used, the incidence of spikes in one SLT study was 25% [24], and in one ALT study 34% of eyes [25].

Heavy pigmentation of the trabecular meshwork has been strongly associated with IOP rises in both types of laser trabeculoplasties. There is a report of a case series by Harasymowycz et al. [22] with persistent elevation of IOP following SLT in eyes with heavily pigmented trabecular meshwork that required trabeculectomy [22]. The risk of such complications may be reduced by decreasing the power or treating less trabecular meshwork [15].

Other complications of laser trabeculoplasty that appear to be seen much less with SLT than ALT include pain during treatment, blurry vision and conjunctival injection. The anterior chamber flare was significantly lower in the SLT group (13.3 SD 6.3 photons/ms) than in the ALT group (20.7 SD 7.4 photons/ms), $P=0.003$ in one study an hour after treatment [18].

There have been reports of some cases that developed corneal edema from 24 hours up to one week after the surgery following SLT. It is not yet understood what may predispose a patient to corneal changes as a result of this procedure, although HSV stromal keratitis reactivation as a result of inflammatory

cascade following laser treatment was attributed in one case. Routine use of topical anti-inflammatory drops may avoid this complication [26,27]. The Glaucoma Laser Trial reported a 46% rate of greater than or equal to 1 degree of peripheral anterior synechiae formation (PAS) after ALT. PAS are extremely rare following SLT treatment [25].

There are also rare complications of SLT reported including transient and uneventful hyphemas [28,29] and a case of severe iritis with choroidal effusion [30]. Unlike ALT, SLT does not destroy the outflow apparatus of the eye that gives the latter theoretical advantages that may include improved response to certain glaucoma medications that rely on improving trabecular outflow, potential for repeat treatment, and preservation of the Schlemm's canal for possible future angle surgery.

Future Directions for Clinical Research

The use of lasers in glaucoma continues to evolve, with a trend towards primary and earlier intervention. Studies suggest a role for SLT as initial therapy for open-angle glaucoma and ocular hypertension and have demonstrated efficacy equal to medical therapy with prostaglandin analogue in one year [31-33]. The advantages of initial laser therapy includes its safety as compared to long term use of medical therapy, compliance to treatment is not an issue and cuts costs related to medical therapy [34]. However, an important risk to mitigate is that patients may get lost to follow-up (some may feel their glaucoma is 'cured') and then return years later with uncontrolled glaucoma. Hence, although more work needs to be done comparing SLT as primary therapy to other modalities of treatment, emphasis should also be given to ensure patients and care partners are well educated about their disease and the importance of regular followup to monitor IOP, optic nerve and retinal nerve fiber layer structure, and visual field function.

In the last decade and a half, SLT has proven to be equally effective as ALT in lowering IOP in primary open angle glaucoma and exfoliation glaucoma; however, future studies need to focus on 180 vs. 360 degree treatment, repeatability (when entire 360 degrees has been treated and additional treatment is being done) and its role, in comparison to ALT and other laser trabeculoplasty methods, in other glaucomas such as pigmentary glaucoma.

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